a rule, noted in all cases of acute leukæmia ending in rapid destruction of the white cells, due to the sepsis or to infection. A. Magnus Levy[19] has recorded the most remarkable phenomenon of this character, viz., 8.72 grammes in twenty-four hours. He also observed in the same case, as well as in a number of other acute cases, that there was a large amount of urine and an increase of total nitrogen and uric acid.

I desire to express my sincere thanks to Dr. Herbert U. Williams for his kind assistance in the preparation of this article, and to Dr. Albert Woehnert for making the blood examinations.

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# A CONTRIBUTION TO CLINICAL OBSERVATIONS ON BLOOD-PRESSURE.

By Herbert Swift Carter, A.M., M.D.,
of New York.

The vagueness which has long surrounded terms used to denote variation in blood-pressure has led men of an inventive turn of mind to devise instruments for determining these variations with some degree of accuracy. Special interest has been aroused within the past few years by a decided advance in such instruments which are of clinical value especially by the sphygmometer devised by Messrs. Hill and Barnard, of St. Bartholomew's Hospital, London, and the tonometer of Gaertner. The results of the experiments detailed in this paper have been determined by means of the sphygmometer; and although not an ideally perfect instrument, the results obtained with it are sufficiently uniform and accurate to be of distinct value in following cases from day to day, in keeping records of blood-pressure, and in making valuable observations. The manometer tubes will not soon be replaced in the experimental laboratory; but, of course, their usefulness is *nil* in gaining knowledge of altered blood-pressure at the bedside, to whatever causes due. The sphygmometer is in reality the manometer tubes reduced to a dial (on the principle of the aneroid barometer) and made practical for clinical use.

For those unfamiliar with the instrument a short description of the main points in its construction and method of use will be of interest.[1]

"It consists of (1) a broad armlet, which is strapped about the upper arm. The armlet is formed of a leather or flexible steel band, on the side of which there is fastened a bag of thin India-rubber. The rubber bag is connected by a Y-tube with (2) a small compressing air-pump fitted with a valve and (3) a pressure gauge. The pressure gauge is of special construction. Roughly, it consists of a metal tambour, the expansion of which is exhibited in a highly magnified form by means of an index or pointer which travels around a dial. This dial is graduated in millimetres of mercury."

*Method of Use.* The armlet, with the rubber bag, is fastened about the arm just above the elbow (or on any part of the arm or leg where it can be made to fit snugly). Air is now forced into the bag by means of the air-pump until the needle begins to move on the dial (there then being a continuous column of air between the bag and the registering mechanism in the pressure gauge). The pulse wave is communicated from the artery to the needle through the column of air already referred to, and is shown by an oscillating movement. The width of the needle's excursion increases with the increasing pressure in the bag until this pressure is equal to the mean arterial pressure, when the excursion of the needle will be at its greatest. The reading in millimetres of Hg on the dial will represent the mean arterial tension. From this point on, with increase of pressure in the bag, the excursion becomes less and less, and finally ceases at a point which corresponds to the maximum arterial pressure. It is, however, only the mean arterial pressure with which we have to do in these experiments.

In order to obtain accurate readings the patient must be at rest in the prone position, as it has been clearly demonstrated by Hill and Barnard:

"1. That the arterial pressure is the same in all the larger arteries while the subject lies horizontally.

"2. In changing from a horizontal to the vertical position the pressure in the upper part of the brachial artery (and it may be assumed also in the carotid artery) either remains constant or becomes slightly elevated.

"3. On changing from the horizontal to the sitting posture the pressure in the arteries of the lower limbs becomes higher than that in the upper limbs by the height of a hydrostatic column of blood separating the two points of observation. If the body remain horizontal and the legs are elevated the converse result holds true."[2]

These results have been proven true in these experiments, except the third point referred to, the correctness of which is assumed from Hill and Barnard's observations. The difference, in the sitting posture, of the mean arterial pressure in brachial and peroneal arteries ranges from 10 to 25 mm. Hg, the average being 17 mm. Hg higher in the latter.

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[1] Hicks. Notes on the Sphygmometer.

[2] Proceedings of the Physiological Society, December 11, 1897.

The armlet is best applied snugly and the reading repeated several times. In a certain number of cases the readings are difficult to obtain, as the oscillations of the needle are very nearly the same over quite a large area—*i. e.*, 5 to 10 mm.; in these the average of several readings must be taken.

Of course, one of the chief advantages of some such method of recording blood-pressure is that it does away with vague terms as "slight," "moderate," or "marked" increase in tension, which necessarily exist where the old method of relying entirely on the touch for one's information is used; for while an individual observer might be able to tell very accurately the relative difference in pressure from day to day, and his interpretation be correct so far as it went, his observations would be of little positive value or have little positive meaning to anyone who could not feel and interpret that particular artery for himself. Hence something definite is conveyed to the mind of anyone reading of a case of nephritis, for example, where the mean arterial pressure is recorded as 150 mm. Hg, knowing the average normal range to be 110 to 120 mm. Hg. Besides which it enables us, in chronic cases associated with increased blood-pressure, to find the drug which will do the maximum of work with the minimum dose—a point of considerable value when it is taken into consideration how long some of these cases require medication.

It is quite without the province of such a paper as this to discuss the various etiological factors in the production of increased arterial tension, and whether such variations are due to changes in the force of the heart's action, contraction of the arteries, thickened or sclerosed arteries, or, again, to direct changes in the composition of the blood itself (aside from the presence of toxic materials which stimulate the vasoconstrictors). For all such discussion one must refer to some of the standard works on the subject. Suffice it to say that changes in arterial pressure are due to any or all of these factors, and no doubt to others not so well recognized. This paper is strictly with reference to determining such changes as exist, from whatsoever cause, in an experimental way, and the modifications of pressure accomplished by certain drugs and procedures.

Of course, clinically, the classes of cases in which information in regard to increased blood-pressure is of the most value are those of nephritis, with or without arterio-sclerosis, and arterio-sclerosis without nephritis; but those cases with lowered arterial pressure are not to be lost sight of, and form an important class by themselves, to be dealt with later.

The number of cases of all descriptions whose blood-pressure was investigated was 129, and the total number of observations on pressure

503. As a routine in every case besides the pressure there was noted the urine examination, the relative amount of arterio-sclerosis present, and the medication in use.

For the normal healthy adult, Hill and Barnard place the average mean arterial pressure in young men at 110 to 120 mm. Hg in the standing position and 100 to 110 in the recumbent. The average pressure for the cases here recorded in the recumbent position was: Males 116 mm. Hg; females, 113 mm. Hg. The highest record of a mean arterial pressure noted was 235 mm. Hg; the lowest, 80 mm. Hg.[1]

For the sake of completeness the subject is divided as follows:

I. Nephritis. (*a*) Acute: without arterio-sclerosis; with arterio-sclerosis. (*b*) Chronic: without arterio-sclerosis; with arterio-sclerosis.

II. Arterio-sclerosis without nephritis: slight; moderate; marked.

III. Effects of some of the arterio-dilators—drugs and phlebotomy.

IV. Blood-pressure in various diseases.

V. Conclusions and résumé.

## I. NEPHRITIS.

### (*a*) *Acute Nephritis.*

| | | *All 9 cases.* | *5 cases uncomplicated.* |
|---|---|---|---|
| With arterio-sclerosis 9 cases. Total number of observations and readings 53. | Highest mean arterial pressure, | 150 mm. Hg. | 150 mm. Hg. |
| | Lowest " " " | 82 " " | 100 " " |
| | Average " " " | 115 " " | 123 " " |

| | | *All 7 cases.* | *There were none uncomplicated.* |
|---|---|---|---|
| Without arterio-sclerosis 7 cases. Total number of observations and readings 50. | Highest mean arterial pressure, | 155 mm. Hg. | |
| | Lowest " " " | 85 " " | |
| | Average " " " | 117 " " | |

A glance at this tabulated series of cases of acute nephritis shows one that, taking them as a whole, the highest, lowest, and average mean arterial pressure of cases of both classes—*i. e.*, with or without arterio-sclerosis—is almost identical. The five cases of nephritis with arterio-sclerosis uncomplicated by any other conditions, such as acute infectious diseases, etc., show an average pressure rather higher than that of all the cases taken together. This is accounted for by the fact that among the latter are included several cases with extremely lowered vitality, such as lobar pneumonias on the sixth to eighth day, marked anæmias, etc. In no case of a secondary parenchymatous nephritis complicating an acute infectious disease was the pressure over 122 mm. Hg, and it was usually much below this, ranging from 84 to 118 mm. Hg.

In all the cases in which arterio-sclerosis was present in conjunction with the nephritis it was slight or of only moderate degree, and in no case were the arteries stiff and hard; then too, that the highest, lowest, and average pressures were practically the same in the two classes of acute nephritis cases—*i. e.*, with or without sclerosis—shows that slight or moderate arterial thickening plays comparatively a small rôle in the production of increased peripheral tension, a point which will be more clearly demonstrated when dealing with cases of arterio-sclerosis as a whole.

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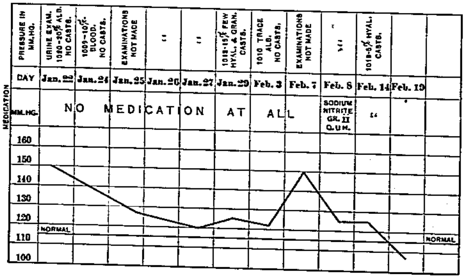
[1] For all discussion in regard to the variations in pressure produced by physiological processes, *e. g.*, sleep, exercise, emotion, etc., one is referred to Oliver's excellent article, Edinburgh Medical Journal, 1898, vol. iv. p. 1.

Another noteworthy fact in regard to these cases is that while we often get a great increase of blood-pressure under any conditions, we may find it normal, or, indeed, subnormal. In the five cases of acute nephritis without other complication than a slight or moderate arterio-sclerosis the average tension was 7 to 10 mm. Hg above the normal range.

It was found on examination of the urine in these cases that, on the whole, the greater the amount of albumin present the higher was the mean arterial pressure. This, however, had some notable exceptions, although they were almost invariably found among the cases with greatly lowered vitality from other causes.

### *Cases of Special Interest.*

CASE XXXVII.—Man, aged twenty-five years. No previous nephritic history. Patient has been a steady and heavy drinker for a number of years. Illness began about ten days previously, with loss of appetite, slight fever, and œdema of legs and face. Complained of very slight dyspnœa on exertion. Urine examination on admission: specific gravity, 1012; 20 per cent albumin. Blood: no casts; mean arterial pressure, 150 mm. Hg. The subsequent run of the case is shown by the accompanying chart:



This case shows the normal decline in blood-pressure which goes hand-in-hand with a spontaneous recovery from an acute diffuse nephritis, and, incidentally, the effect of one of the most reliable arterio-dilators. On one occasion there was an abrupt rise in pressure of about 30 mm. Hg without known cause. This fell promptly to normal as soon as sodium nitrite—2 grains every four hours—was given the patient.

There is one case of interest, showing, as it does, the return to normal from a lowered blood-pressure, as the result of exhaustion, on the ninth day, of a lobar pneumonia. The pressure then was 98 mm. Hg. Three days later—*i. e.*, after defervescence—pressure 105; and seven days later pressure 120 mm. Hg, while the patient's general condition had improved with tonics only as medication, the urine in the meantime becoming normal. The nephritis in this case only amounted to a slight transient albuminuria (1 per cent.), due to the acute parenchymatous degeneration complicating the pneumonia.

Further than these observations there was nothing of particular interest to note except the effects of medication on lowering pressure in these cases and a comparison of the averages with those of the cases of chronic nephritis with arterial sclerosis and those of arterial sclerosis without nephritis. This may be done at a glance, the points of comparative interest being brought out in the résumé.

(*b*) *Chronic Nephritis.*

| | | *All 26 cases.* | *19 cases uncomplicated.* |
|---|---|---|---|
| With arterio-sclerosis 26 cases.<br>Total number of observations and readings 168. | Highest mean arterial pressure, | 235 mm. Hg. | 235 mm. Hg. |
| | Lowest " " " | 85 " " | 112 " " |
| | Average " " " | 177 " " | 187 " " |
| Without arterio-sclerosis. | No cases seen. | | |

There were twenty-six of these cases of chronic nephritis observed, and all were complicated by an arterio-sclerosis of varying degree, there being none seen without it; and so far, as so limited a number of cases can, it shows that with chronic nephritis it is the rule to find this complication. However, as we shall see, the converse is not true, for many cases of arterio-sclerosis were observed without evidences of nephritis.

In looking over the cases as a whole the highest pressure found—235 mm. Hg—was in a case in which the urine showed a specific gravity of 1014, with 10 per cent. of albumin without casts, but complicated by one of the most extreme degrees of arterio-sclerosis found. No doubt here the sclerosis was much more the cause of the high pressure than the nephritis, the patient being comparatively comfortable in spite of it. This comparative comfort was usual in the arterio-sclerosis cases.

The lowest mean arterial pressure seen in this class was 85 mm. Hg, and was in a case of chronic diffuse nephritis in which the urine examination was quite unexpected. The specific gravity ranged from 1012 to 1031; the albumin 60 to 99 per cent., with a few hyaline and granular casts, and the patient passing 41 to 104 ounces of urine in the twenty-four hours. Here, however, the arterio-sclerosis was very slight; but it shows that a low arterial pressure may accompany a nephritis of considerable extent. In only one case of the series was the pressure found lower, and that was in the case already referred to with pericarditis, rheumatism, and anæmia—pressure 82 mm. Hg. In the acute case as well the arterio-sclerosis was extremely slight.

A comparison of the pressures in these cases of chronic nephritis with those found in the acute condition shows the highest and average mean arterial pressure to be much higher in the former, the average mean arterial pressure being 62 mm. Hg higher in the chronic form. There is comparatively little difference in the lowest pressures to be found in each, either complicated or uncomplicated (arterio-sclerosis is ignored as a complication in this connection).

After careful examination of the data it is found that blood-pressure, urine examination, and the amount of arterio-sclerosis seem to bear no definite relation to each other beyond the fact that marked arterio-sclerosis complicating the nephritis increases the pressure.

### *Chronic Nephritis—Cases of Special Interest.*

CASE L. was of interest as showing the lowering of blood-pressure during the period of apnœa in a patient with Cheyne-Stokes respiration in the terminal stages of chronic nephritis with chronic uræmia. Pressure after several deep inspirations, 140 mm. Hg; during apnœa, 125 mm. Hg. This difference was also appreciable to the finger, although the exact amount could not be accurately gauged in that way.

CASE LXXIX. illustrates the low pressure in cases of aortic regurgitation complicated by chronic nephritis. Patient, aged forty-five years; suffering from chronic nephritis. Urine: specific gravity, 1017; 20 per cent. albumin; granular and hyaline casts. Pressure, 85 mm. Hg. As will be shown under "Endocarditis," low pressure is the rule for aortic regurgitation, with or without nephritis or other complications, save where there is an accompanying mitral regurgitation.

CASE LXXXIV.—Acute pericarditis and articular rheumatism. Chronic nephritis; anæmia. Blood-pressure, 82 mm. Hg. Pericardium tapped; 3 ounces of bloody fluid obtained. After tapping, pressure 82 mm. Hg. No effect on blood-pressure whatever.

Under heading on "Effect of Drugs" other points of interest about these cases of chronic nephritis will be brought out.

## II. ARTERIO-SCLEROSIS WITHOUT NEPHRITIS.

| | | | |
|---|---|---|---|
| | | *All 18 cases.* | *7 uncomplicated cases.* |
| Slight arterio-sclerosis 18 cases. 36 observations and readings. | Highest mean arterial pressure, | 128 mm. Hg. | 122 mm. Hg. |
| | Lowest " " " | 80 " " | 104 " " |
| | Average " " " | 107 " " | 112 " " |
| | | *All 14 cases.* | *7 uncomplicated cases.* |
| Moderate arterio-sclerosis 14 cases. 28 observations and readings. | Highest mean arterial pressure, | 130 mm. Hg. | 125 mm. Hg. |
| | Lowest " " " | 80 " " | 108 " " |
| | Average " " " | 107 " " | 116 " " |
| | | *All 4 cases.* | *2 uncomplicated cases.* |
| Marked arterio-sclerosis 4 cases. 43 observations and readings. | Highest mean arterial pressure, | 205 mm. Hg. | 205 mm. Hg. |
| | Lowest " " " | 130 " " | 138 " " |
| | Average " " " | 165 " " | 174 " " |

Total averages for the thirty-seven cases of arterio-sclerosis of all degrees without nephritis: highest, 205; lowest, 80; average, 131 mm. Hg.

The divisions into slight, moderate, and marked arterio-sclerosis are, of course, merely arbitrary and determined by touch, and as such cannot be supposed to be exact; but after feeling a great many vessel walls one naturally divides the relative amount of thickening into these three classes, and although the limits of each are not clear-cut, still for practical purposes they are accurate enough.

By uncomplicated cases are meant all cases of arterio-sclerosis pure and simple, without acute conditions or valvular endocardial lesions, both of which are found at times to modify the arterial pressure.

A ready comparison may be made of arterial pressure between these classes of cases taken as a whole, or the uncomplicated alone, on referring to the foregoing classification. Referring only to the uncomplicated cases in each class, it is easily seen that the highest mean arterial pressure of cases with slight or moderate arterio-sclerosis is practically the same, the variation being only 3 mm. Hg in favor of the latter; the same holding true for the lowest and average pressures of the two classes, the average pressure in both being practically that of the normal individual. On the other hand, when we look at the pressures of the cases with marked arterio-sclerosis we see a great increase in all three, the average pressure being 58 to 62 mm. Hg higher than in the cases with a slight or moderate sclerosis. This is such a definite fact that it may with safety be laid down as a rule, that it is only an arterio-sclerosis of marked degree that, unaided by other conditions, increases to any extent the blood-pressure in the peripheral circulation. The same increase is shown in the cases taken as a whole, complicated and uncomplicated alike.

This failure of slight or moderate sclerosis to modify the arterial pressure was also shown in the cases of acute nephritis, to which the reader is referred.

The general idea gained in looking over standard works which treat of circulatory conditions in disease is that arterial thickening in general causes an increase in the blood-pressure of the individual—*i. e.*, no distinction is made as to the amount of the sclerosis necessary to cause such a result. This may be true theoretically, and to some extent practically, so far as the internal blood-pressure is concerned, but as yet we have no means of estimating such a condition if it really exists; certainly the peripheral blood-pressure is not materially increased except in cases in which the sclerosis is extreme. The number of cases of slight or moderate arterio-sclerosis in this series seems large enough to formulate the foregoing rule with safety. Those cases which were of especial interest in these classes will be discussed under the head of their associated complications. None of the cases of straightforward, uncomplicated arterio-sclerosis were of particular interest.

## III. Effect of some Drugs and Procedures Used in the Reduction of Increased Arterial Pressure.

Clinically, the effects of medication are often perfectly plain, and we do not need the evidence of any new method, such as sphygmometry, to convince ourselves that certain arterio-dilators do good under certain conditions associated with increased peripheral blood-pressure. What is of interest, however, in this connection is:

1. How much effect do these drugs really have, measured by some definite means?
2. How promptly do they act?
3. How long does their action continue?

As this series of experiments is only meant to be a contribution to the study of the effects of some of the arterio-dilators, exhaustiveness is not claimed, but further knowledge is to be gained by future investigation.

It has been a difficult matter to determine satisfactorily, in many instances, what particular drug had the most marked effect in the reduction of blood-pressure, even with the aid of an instrument, and the results of observation here given have been determined with much difficulty. In order to obtain results as uniform as possible, with few exceptions the observations were made at the same time of day, viz., between 2 and 5 P.M., so that taking of food, exercise, etc., should not play a rôle in the variations, the patients being at rest in bed.

As will be seen by reference to the tables, the promptness of the drug's action and its duration was noted, while in others the general continued effect was observed. It has also been attempted to show the direct effect of medication and the pressure before administration of the drug; afterward the length of time before the maximum effect was produced, the duration of effect of a single dose, and any clinical points of interest about the cases, drawing conclusions, so far as possible, as to efficacy.

*Erythrol Tetranitrite.* In two cases the drug was given by the mouth, ½ grain t. i. d.

First case, marked arterio-sclerosis. Pressure before administration, 150 mm. Hg; after twenty-four hours' use, pressure 140 mm. Hg.

Second case, chronic nephritis, with marked arterio-sclerosis. Pressure before, 145 mm. Hg; after twenty-four hours' use, pressure 135 mm. Hg.

Erythrol tetranitrite reduced pressure in each case 10 mm. Hg. The drug is too expensive for general use and not as effectual as sodium nitrite.

### NITROGLYCERIN. SERIES OF TWELVE CASES.

| No. | Diagnosis. | Dose of nitroglycerin. | How given. | Pressure before. | Pressure after. | Effect noted in | Amount. | Effect lasted | Pressure returned to | Urine examination. | Amount of arteriosclerosis. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Chronic nephritis, acute exacerbation, | Gr. 1/600 every 2 hrs. | By mouth | 155 mm. Hg. | 125–130 mm. Hg. | Within 24 hours. | 25–30 mm. Hg. | Continued to fall during convalescence. | ......... | 1028, 25 per ct. casts;<br>1020, 2 per ct. in two days. | Slight. |
| 2 | Acute nephritis, | Gr. 1/100 every 2 hrs. | Hypo. | 155 " " | 130 mm. Hg. | Within 24 hours. | 25 mm. Hg. | Four days, while on drug. | Continued to fall. | 1025, 60 per ct. blood casts;<br>1010 trace casts. | None. |
| 3 | Abdominal tumor, | Gr. 1/100 once. | Hypo. | 122 " " | 115 " " | 9 min. | 7 " " | 1½ hours. | Not seen. | 1021, o. k. | None. |
| 4 | Acute nephritis, | Gr. 1/60 once. | By mouth. | 118 " " | 105 " " | 20 " | 13 " " | 1 hr. 20 min. | 115 mm. Hg. | 1018, 2 per ct. casts and blood. | Slight. |
| 5 | Cirrhosis of liver, | Gr. 1/60 once. | By mouth. | 115 " " | 110 " " | 15 " | 5 " " | About 1 hour. | 115 " " | 1015, hyaline casts. | Slight. |
| 6 | Chronic nephritis, acute exacerbation, | Gr. 1/60 once. | Hypo. | 150 " " | 135 " " | 15 " | 15 " " | 1 hour. | 150 " " | 1020, 80 per ct. casts and blood. | Slight. |
| 7 | Lobar pneumonia, chronic nephritis, | Gr. 1/100 once. | By mouth. | 150 " " | 150 " " | None. | 0 | 0 | ......... | 1017, 80 per ct. casts. | Moderate. |
| 8 | Marked arteriosclerosis, | Gr. 1/100 once.<br>Gr. 1/100 every 1 hr. | Hypo<br>Mouth. | 200 " "<br>200 " " | 200 " "<br>200 " " | None.<br>None. | 0<br>0 | 0<br>0 | ......... | 1026, negative. | Marked. |
| 9 | Chronic nephritis, | Gr. 1/100 every 2 hrs. | Hypo. | 122 " " | 122 " " | None. | 0 | 0 | ......... | 1020, 5 per ct. casts. | Moderate. |
| 10 | Gastroduodenitis, jaundice, | Gr. 1/60 once. | By mouth. | 105 " " | 105 " " | None. | 0 | 0 | ......... | 1020, negative. | None. |
| 11 | Lobar pneumonia, | Gr. 1/100 every 4 hrs. | By mouth. | 108 " " | 111 " " | None. | 0 | 0 | ......... | 1030, negative. | Slight. |
| 12 | Chronic nephritis, | Gr. 1/100 every 2 hrs. | By mouth. | 112 " " | 112 " " | None. | 0 | 0 | ......... | 1016, 80 per ct. casts. | Moderate. |

*Conclusions.* 1. Continued effect of $\frac{1}{100}$ grain, by the mouth or hypodermically, results in lowered pressure, sometimes very good, and reduction may be greater than after a single dose under similar conditions. This is a fact in clinical experience where tension is high—*e. g.*, Cases I and II.; uncertain where tension is moderate—*e. g.*, Case IX.

2. The direct effect of a single dose of $\frac{1}{100}$ grain hypodermically is uncertain, sometimes resulting in moderate reduction of pressure—*e. g.*, Case III.—or is ineffectual. Case VII. (here the patient died in uræmic convulsions, phlebotomy even failing to reduce pressure).

3. The direct effect of a single dose of $\frac{1}{50}$ grain is reliable, with moderate lowering of pressure—5 to 15 mm. Hg.—in fifteen to twenty minutes. The promptness of action is about the same whether given by the mouth or hypodermically—*e. g.*, Cases IV., V., and VI.

4. The average duration of the positive effect from any dose is one hour and twelve minutes. No lowering of pressure when increase is due to marked arterio-sclerosis, either by a single dose of $\frac{1}{100}$ grain hypodermically or continued every hour by the mouth—*e. g.*, Case VIII. When pressure is already subnormal no further lowering follows the use of a single dose of grain $\frac{1}{100}$, or every two hours or every four hours—*e. g.*, Cases X., XI., and XII.

*Résumé of Cases Given Sodium Nitrite.* Dosage, ½ to 3 grains, always by the mouth.

CASE XIII.—Most marked reduction of pressure in case of extreme arterio-sclerosis—50 mm. Hg. (This was repeated with identical results.)

Taking the other cases with positive results we find: Pressure lowered 10 to 15 mm. Hg; average, 12.2 mm. Hg. Effect evident in ten to fifty minutes; average, twenty-six minutes. Effect lasted one and a half to two hours; average, one hour and forty minutes.

The cases were acute or chronic nephritis, with more or less arterio-sclerosis, and one case of marked arterio-sclerosis without nephritis. One negative result. The case was a chronic nephritis, with an acute exacerbation and uræmic convulsions, and required phlebotomy, sodium nitrite having no effect.

*Conclusions.* Sodium nitrite reduces arterial pressure promptly, and is usually best given in doses of 2 to 3 grains every two to four hours, depending on the urgency of the symptoms. According to these experiments this is the most satisfactory and reliable arterio-dilator, and acts whether the increased pressure is due either to nephritis or arterio-sclerosis. As with nitroglycerin, continued use in some cases shows greater effect than a single dose. No depressing effects on the patient's general condition were seen.

*Potassium Iodide.* Four cases tested. Dosage, 10 grains t. i. d. in three cases, and 5 grains every four hours in one case. No effect from either could be discovered by the sphygmometer.

SODIUM NITRITE. SERIES OF ELEVEN CASES.

| No. | Diagnosis. | Dose of sodium nitrite. | How given. | Pressure before. | Pressure after. | Effect noted in | Amount of reduction. | Effect lasted | Pressure returned to | Urine examination. | Amount of arteriosclerosis. |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 13 | Marked arteriosclerosis, | Gr. ij every 4 hrs. | By mouth. | 200 mm. Hg. | 150 mm. Hg. | Within 4 hours. | 50 mm. Hg. | While taking drug. | 200 mm. Hg. 3 hrs. after last dose. | 1026, negative. | Marked. |
| 14 | Normal case, | Gr. j every 4 hrs. | " " | 110 " " | 95 " " | 8 hrs after first dose; not seen before. | 15 " " | Not noted. | ......... | 1032, negative. | Moderate. |
| 15 | Acute nephritis, | Gr. ij once. | " " | 125 " " | 112 " " | 30 minutes | 13 " " | 2 hours. | 125 mm. Hg. | 1011 trace alb. gran. casts. | Moderate. |
| 16 | Acute nephritis, | Gr. ij once. | " " | 128 " " | 112 " " | 50 " | 13 " " | 2 hours. | 128 " " | 1011, trace, casts. | Moderate. |
| 17 | Acute nephritis, | Gr. ij once. | " " | 128 " " | 112 " " | 10 " | 13 " " | 1 hr. 50 min. | 128 " " | 1027, 3 per ct. albumin, hyal. casts. | Slight. |
| 18 | Chronic nephritis, | Gr. ½ once. | " " | 122 " " | 110 " " | 15 " | 12 " " | 1 hr. 30 min. | Not noted. | 1018, 3 per ct. albumin, no casts. | Moderate. |
| 19 | Chronic nephritis, | Gr. iij once, & every 4 hs. | " " | 155 " " | 140 " " | 26 " | 15 " " | 1 hr. 30 min. | 155 mm. Hg. | 1017, trace, no casts. | Marked. |
| 20 | Chronic nephritis, acute exacerbation, | Gr. ij every 4 hrs. | " " | 155 " " | 155 " " | 0 | ......... | ......... | ......... | 1028, 75 per ct. albumin, casts. | Slight. |
| 21 | Chronic nephritis, | Gr. iij once, & every 4 hs. | " " | 150 " " | 140 " " | 15 minutes | 10 mm. Hg. | 1 hr. 35 min. | 150 mm. Hg. | 1035, 5 per ct. casts. | Moderate. |
| 22 | Chronic nephritis, | Gr. ij every 4 hrs. | " " | 150 " " | 140 " " | Not seen until next day. | 10 " " | ......... | ......... | 1015, 35 per ct. casts. | Moderate. |
| 23 | Chronic nephritis, | Gr. ij every 4 hrs. | " " | 122 " " | 110 " " | Not seen until second day. | 12 " " | While taking drug. | ......... | 1020, 5 per ct. albumin casts. | Moderate. |

*Chloral Hydrate.* Three cases tested. Dose, 5 grains every four hours in all the cases. Diagnosis: Marked arterio-sclerosis; acute nephritis; chronic nephritis. No effect could be discovered. Tests were not conclusive.

*Spiritus Etheris Nitrosi.* Two cases. Dosage, ½ drachm, every four hours. No effect discovered.

PHLEBOTOMY AND INTRAVENOUS INFUSION OF HOT NORMAL SALT SOLUTION. TABLE OF FIVE CASES.

| No. | Diagnosis. | Am't of blood withdrawn. | Am't of saline infusion. | Pressure before the operation | Pressure after the operation | Amount of fall in the blood pressure. | Remarks and notes on cases. |
|---|---|---|---|---|---|---|---|
| 29 | Chronic nephritis. | Oz. v. | 1500 c.c. at 114° F. | 200 mm. Hg. | 150 mm. Hg. next day. | 50 mm. Hg. | Marked general improvement; urine 1019, 30 per cent. albumin; casts. |
| 66 | Chronic nephritis. | Oz. viij. | 1400 c.c. | 195 mm. Hg. | 150 mm. Hg. 3 days later. | 45 mm. Hg. | Marked general improvement; urine 1013, 5 per cent. albumin; casts. |
| 97 | Chronic nephritis, marked arterio-sclerosis. | Oz. viij. | 1200 c.c. | 180 mm. | 170 mm. next day. | 10 mm. Hg. | The extreme arterio-sclerosis probably had much to do in preventing more complete fall of pressure; clinically patient much better next day, although tension still high. |
| 40 | Chronic nephritis. | Oz. vj. | 1500 c.c. | 122 mm. | 122 mm. 6 hours after. | 0 | General condition much improved, although tension not lowered; urine 1020, 5 per cent. hyal. and gran. casts. |
| 31 | Chronic nephritis, convulsions. | Oz. xv. | 1500 c.c. | 125 mm. | 125 mm. | 0 | Condition improved, though pressure not lowered; urine 1016, 20 per cent. alb.; red-cells. |

*Conclusions.* Phlebotomy and saline infusion are good in all cases with markedly increased tension and where patient's condition is serious as a result of uræmic poisoning. In some cases blood-pressure is decidedly lowered, and in all there is marked improvement in the patient's general condition, even where no lowering of blood-pressure can be detected.

*Effect of Extract of Suprarenal in Increasing Blood-pressure.* Six cases. Dose, 5 grains, t. i. d. and every four hours. Results were the same in either dosage. Positive results in five cases. Pressure increased 2 to 10 mm. Hg; average, 6.6. mm. Hg. The effect was usually evident after two doses had been taken, and lasted while the drug was exhibited. One negative result. Case received 5 grains t. i. d. and every four hours. No effect was discovered, although the drug was continued for five days. In all these cases the blood-pressure was normal or subnormal before medication.

The positive effects of extract of suprarenal in increasing the blood-pressure are sufficiently marked to open the way for a wider field of usefulness for the drug in conditions representing a lowered vascular tone. Its local effects are so well known that nothing need be said for its local vasoconstrictor stimulative power, but much wider experiment is needed to decide of just how much use it can be in conditions where it is desirable to increase the general blood-pressure.

## IV. Notes on Blood-pressure in Various Diseases Other than Nephritis or Arterio-sclerosis.

*Endocarditis—Valvular Lesions.* One learns very little in regard to the working capacity of the heart by sphygmometry; and in no way can the sphygmometer compare with the sphygmograph for this purpose, for it is remarkable how serious a valvular lesion may exist and how desperately ill a patient may be and still have practically a normal blood-pressure. A striking example of this was a patient with double aortic lesion and mitral insufficiency, who was clinically in great distress, sitting upright in bed, breathing with difficulty, the heart markedly dilated and hypertrophied, in whom the arterial pressure was 115 mm. Hg—*i. e.*, normal.

The two points worthy of mention under this heading are: 1. The low pressure seen in cases of aortic regurgitation uncomplicated by any mitral lesion. Three cases of this kind were observed with pressures of 80, 85, and 85 mm. Hg, respectively; the regurgitation was undoubted. 2. The compensation (so far as pressure is concerned), in some cases of aortic regurgitation, by a mitral insufficiency.

Cases with aortic regurgitation and mitral insufficiency: (1) One with mean arterial pressure of 115 mm. Hg. (2) One with mean arterial pressure of 110 mm. Hg. (3) One with mean arterial pressure of 155 mm. Hg (complicated by nephritis).

The last case shows that the blood-pressure may be even away above normal in these cases if complicated by nephritis.

*Lobar Pneumonia.* There were twelve cases observed, and notes on pressure of the blood taken on the second, third, fourth, fifth, sixth, seventh, eighth, ninth, and tenth days. Nothing definite was discovered in regard to a continued rise or fall of pressure during the progress of the disease. Cases which showed a low pressure after the crisis (and this was quite frequently true) also showed a steady rise to normal pressure during convalescence. Observations of prognostic value were not made.

*Anæmia (Primary).* It was an interesting fact noted in this class that the blood-pressure was almost invariably lowered unless complicated by a nephritis or marked arterio-sclerosis. This is quite contrary to such authority as Oliver, who states that in chlorosis and anæmia mean arterial pressure is, as a rule, raised, but the rise is generally but moderate in degree.[1]

TABLE OF CASES OF ANÆMIA.

| Case. | Hæmoglobin. | Complication (if any). | Mean arterial pressure. |
|---|---|---|---|
| 1 | 60 per cent. | Gastric ulcer | 82 mm. Hg. |
| 2 | 62 " | Acute rheumatism | 82 " " |
| 3 | 40 " | Gastric ulcer | 84 " " |
| 4 | 65 " | Gastric ulcer | 85 " " |
| 5 | 48 " | None | 85 " " |
| 6 | 65 " | None | 85 " " |
| 7 | 55 " | Gastric ulcer | 85 " " |
| 8 | 60 " | None | 95 " " |
| 9 | 65 " | None | 95 " " |
| 10 | 40 " | Gastric ulcer | 95 " " |
| 11 | 60 " | Catarrhal jaundice | 105 " " |
| 12 | 45 " | Gastric ulcer and acute nephritis | 108 " " |
| 13 | 85 " | None | 110 " " |

The only exception to this almost invariable rule of low pressure associated with anæmia is in Case XIII., and here the hæmoglobin was 85 per cent., or at least 20 per cent. higher than in any of the other cases; this percentage of hæmoglobin is so nearly that which is ordinarily found in most individuals as normal that it seems fair to class it as such. The accompanying nephritis in Case XII. accounts for the pressure—108 mm. Hg—with low hæmoglobin. No accurate relation between the amount of hæmoglobin and the mean arterial pressure could be discovered.

*Gastric Ulcer.* There were five cases of this condition observed, all complicated by a greater or less degree of anæmia. The blood-pressure ranged from 82 mm. Hg to 100 mm. Hg, the average being 87 mm. Hg. The hæmoglobin, estimated by Von Fleischl method, ranged from 55 per cent. to 70 per cent., the average being 67 per cent.

The thought which naturally arises in this connection is: Could not the lowered pressure, which we find almost always accompanies an anæmia, be a factor in the production of gastric ulceration? for, as is well known, nearly all the cases of ulceration show signs of anæmia before the symptoms of ulceration develop; at least, it seems that this may in some cases be proved to play a rôle in the production of gastric ulcer—*e. g.*, lowered pressure in the capillaries of the mucosa, partial or complete stasis in some, and diminished vitality of the part, with autodigestion at this point, resulting in ulceration.

No mention of such etiological factor can be found in any of the numerous general and special treatises on the subject consulted, but it offers at least a field for investigation.

*Typhoid.* Three cases. All showed lowered pressure when accompanied by high temperature.

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[1] G. Oliver. Blood and Blood-pressure, 1901, p. 261.

*Other Cases Noted.* Trichinosis; cirrhosis of liver; acromegaly; Raynaud's disease; epilepsy; bronchitis, with or without asthma; rheumatism, acute or chronic; rheumatic purpura; tertian malaria; tubercular peritonitis; sciatica. In none of these cases was there anything abnormal found in regard to blood-pressure.

## V. Résumé and Conclusions.

1. Average normal mean arterial pressure is: males, 116 mm. Hg; females, 113 mm. Hg.

2. In acute nephritis the accompanying arterio-sclerosis, if present, is of slight or moderate degree.

3. In acute nephritis the height of the blood-pressure varies, for the most part, directly with the amount of albumin in the urine.

4. An acute parenchymatous nephritis complicating an acute infectious disease causes little or no increase in blood-pressure.

5. The average mean arterial pressure in chronic nephritis is about 62 mm. Hg higher than that of acute nephritis.

6. There were no cases of chronic nephritis seen without an accompanying arterio-sclerosis.

7. In arterio-sclerosis it is only those cases in which it is extreme that the average mean arterial pressure is raised.

8. The most satisfactory drug for lowering blood-pressure, whether increase is due to nephritis or marked arterio-sclerosis, is sodium nitrite, best given in 2 to 3 grains every two to four hours. It acts in about twenty-six minutes, causing a reduction of 10 to 15 mm. Hg (in marked arterio-sclerosis sometimes much more), the effect lasting one hour and forty-four minutes on the average.

9. When the blood-pressure is high and is accompanied by symptoms of uræmia the best method of rapid reduction is phlebotomy—5 to 8 ounces, followed by saline infusion (1400 to 1500 c.c. of hot normal salt solution) and sodium nitrite in full doses. Clinically, also, there is almost invariably improvement.

10. Blood-pressure in aortic regurgitation, whether complicated by nephritis or not, is low. If a mitral regurgitation is also present pressure may be nearly normal.

11. Blood-pressure in all forms of anæmia is below normal.

12. Possible relation between lowered pressure in chlorosis and the production of gastric ulcer.

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